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Quinolinium Dichromate Oxidation of Diols: A Kinetic Study

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Quinolinium dichromate (QDC) in water oxidizes vicinal and nonvicinal diols to the corresponding α-hydroxy carbonyl compound. The rate is proportional to the concentrations of diol, oxidant and hydrogen ions, and the reactions proceed almost twice as fast in D_2O than in H_2O. These data can be correlated with a mechanistic pathway involving the intermediate formation of a chromate ester, which undergoes decomposition to give the product.

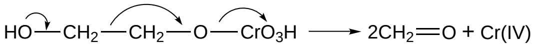
Introduction

The unique feature of chromic acid is that it is able to effect both normal oxidation and cleavage, in so far as its reactions with diols. For example, Waters had reported 1−2% cleavage in the case of ethylene glycol, and 20−30% cleavage of 2,3-butanediol,[1] while Chatterjee and Mukherjee had shown that pinacol was readily cleaved to give acetone.[2] Two mechanistic pathways were thus available:

(i) A normal oxidation to yield an α-hydroxy carbonyl compound such as

$$\mathrm{HOCH_2CH_2OH} + \mathrm{HCrO_4^-} + \mathrm{H^+} \rightleftharpoons \mathrm{HOCH_2CH_2OCrO_3H} + \mathrm{H_2O}$$
$$\mathrm{HOCH_2CH_2OCrO_3H} \rightarrow \mathrm{HOCH_2CHO} + \mathrm{Cr(IV)} \quad (1)$$

(ii) Cleavage of the carbon−carbon bond,



$$\mathrm{HO{-}CH_2{-}CH_2{-}O{-}CrO_3H} \longrightarrow \mathrm{2CH_2{=}O} + \mathrm{Cr(IV)} \quad (2)$$

Rocek and Westheimer had used energy considerations to ascertain the pathway of oxidation and had established that the oxidation to a hydroxy aldehyde (or ketone) was energetically favored by 15 kcal/mol or more.[3] The obvious conclusion was that when a mechanistic pathway was available, the oxidation of a primary or secondary alcohol group to a carbonyl would be preferred to cleavage of the diol.

The stereoselective synthesis of enantiomerically pure α-hydroxy carbonyl compounds has become significant,[4] especially since these compounds have been established as important synthons in the asymmetric synthesis of natural products and fine chemicals.[5,6] It has been shown that the osmium-catalyzed asymmetric dihydroxylation of enol ethers[7] or silyl enol ethers[8] had yielded α-hydroxy ketones in high enantiomeric excess.

While supplementing the earlier work in this area, we have attempted to use kinetic data to help decide which of the two mechanisms, eq 1 or 2 above, would be prevalent in the oxidation reactions of diols by QDC.

We report here the kinetic aspects of the selective conversion of *trans*-1,2-cyclohexanediol and 1,5-pentanediol to the corresponding α-hydroxy carbonyl compound, using quinolinium dichromate (QDC) in acid medium.

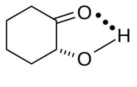
Experimental Section

(a) Materials. The diols (*trans*-1,2-cyclohexanediol and 1,5-pentanediol) were obtained from the Aldrich Co. and were used after recrystallization and distillation, respectively. Quinolinium dichromate (QDC) was prepared by the reported method,[9] and its purity was checked by estimating Cr(VI) iodometrically. Sulfuric acid (E. Merck) was used as such after a check of its physical constants. Acetic acid (E. Merck) was distilled, and the fraction distilling at 116 °C was used.

(b) Kinetic Measurements. The reactions were performed under pseudo-first-order conditions, maintaining a large excess of the diols with respect to QDC. The reactions were carried out at constant temperature (±0.1 K) and were followed by monitoring the UV-vis absorption band at 440 nm, spectrophotometrically, as described in earlier papers.[10−11] All the reactions were performed under nitrogen. The rate constants were evaluated from the linear ($r > 0.995$) plots of log [QDC] against time. The values reported were the mean of two or more runs and were reproducible to within ±3%. The solvent was water or a water−acetic acid mixture. The reaction mixture remained homogeneous in the solvent systems used.

(c) Product Analysis. Using the same experimental conditions as were employed for the kinetic determinations, the reaction mixture was kept overnight for completion of the reaction.

(i) Oxidation of 1,2-Cyclohexanediol. The reaction product was extracted with ether, and the solvent ether was removed. The product was recrystallized from ethanol (mp 113 °C, yield ~90%). IR spectrum of this product showed a sharp band at 1687 $\mathrm{cm^{-1}}$, suggesting the presence of a hydrogen bonded carbonyl group. The absorption band at 3050 $\mathrm{cm^{-1}}$ was due to the presence of the OH group. The lowering in the wave-number of the O−H absorption band was probably due to the presence of hydrogen bonding between the hydroxyl and the carbonyl groups, thus



The product was thus confirmed as 2-hydroxycyclohexanone. The phenylhydrazone derivative of the product was prepared, recrystallized from ethanol, and dried (mp 121 °C).

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Table 1. Dependence of Rate Constants on Oxidant Concentration ([Diol] = 0.01 M; [H_2SO_4] = 1.0 M; *T* = 323 K)

10^4[QDC] (M)	1.0	5.0	7.5	10.0	20.0
10^4k_1 (s^{-1}) for					
1,2-cyclohexanediol	7.75	7.52	7.36	7.67	7.62
1,5-pentanediol	3.96	3.79	3.86	3.93	3.76

Table 2. Dependence of Rate Constants on Substrate Concentration ([QDC] = 0.001 M; [H_2SO_4] = 1.0 M; *T* = 323 K)

10^2[diol] (M)	1.0	2.5	5.0	7.5	10.0	20.0
10^4k_1 (s^{-1}) for:						
1,2-cyclohexanediol[a]	7.67	19.2	38.5	58.0	77.1	155
1,5-pentanediol[b]	3.93	9.81	19.7	29.7	39.6	79.0

[a] 10^2k_2 (M^{-1} s^{-1}) = 7.68 (av). [b] 10^2k_2 (M^{-1} s^{-1}) = 3.94 (av). $k_2 = k_1$/[diol].

(ii) Oxidation of 1,5-Pentanediol. The reaction product was extracted with ether, and the solvent ether was removed. The product (5-hydroxypentanal) was treated with 2,4-dinitrophenylhydrazine in 2 M HCl and left overnight to obtain the corresponding 2,4-dinitrophenylhydrazone (DNP) derivative, which was then filtered and recrystallized from ethanol (mp 80 °C, yield ~90%).

Results

The oxidation of the diols by QDC resulted in the formation of the corresponding α-hydroxy carbonyl compound. Under the present experimental conditions, there was no further oxidation of the product.

Stoichiometry. The stoichiometric experiments were performed under nitrogen at 323 K, under the conditions of $[QDC]_0 > [diol]_0$, at varying acid concentrations. The disappearance of Cr(VI) was followed until the absorbance values became constant. The $[QDC]_\infty$ was estimated. Stoichiometric ratios, Δ[QDC]/Δ[diol], in the range 0.65−0.69 were observed, which conformed to the overall equations:

$$\underset{\text{1,2-cyclohexanediol}}{3C_6H_{12}O_2} + 2Cr^{VI} \rightarrow 3\,C_6H_{10}O_2 + 2Cr^{III} + 6H^+ \tag{3}$$

$$\underset{\text{1,5-pentanediol}}{3C_5H_{12}O_2} + 2Cr^{VI} \rightarrow 3C_5H_{10}O_2 + 2Cr^{III} + 6H^+ \tag{4}$$

Rate Law. Under pseudo-first-order conditions, the individual kinetic runs were first order with respect to QDC. Further, the pseudo-first-order rate constants (k_1) did not vary with the initial concentration of QDC (Table 1). The order with respect to the concentrations of diols was unity (Table 2). The reaction was catalyzed by acid, and the acid-catalyzed reaction showed a first-order dependence on acidity (Figure 1). These data suggest the following rate law:

$$-d[QDC]/dt = k[diol][QDC][H^+] \tag{5}$$

Solvent Isotope Effect. All the oxidation reactions have been carried out in aqueous medium. The effect of a change in the solvent from H_2O to D_2O was studied in order to ascertain the extent of the solvent isotope effect. The rates of oxidation of the diols were increased in D_2O medium by a factor of 2.0 (Table 3).

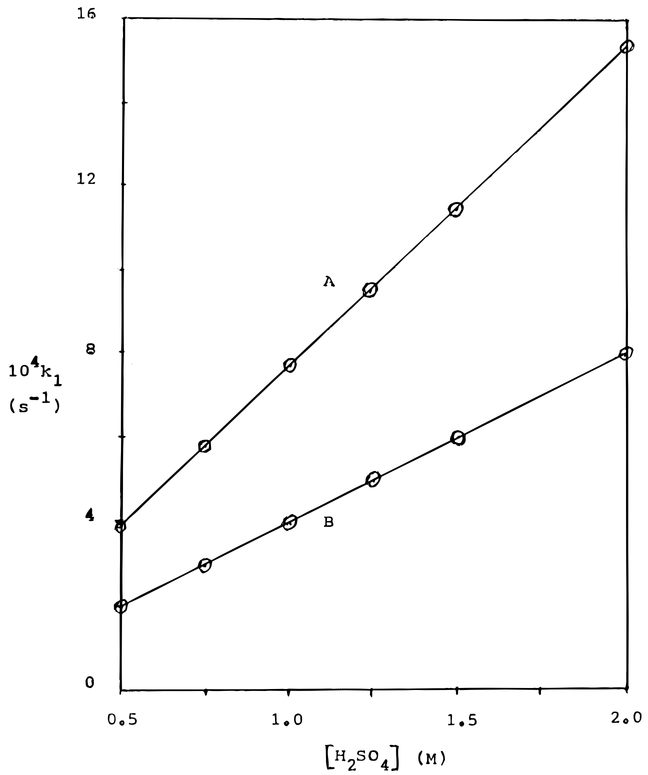


Figure 1. Plot of k_1 vs concentration of H_2SO_4 for 1,2-cyclohexanediol (A) and 1,5-pentanediol (B).

Table 3. Solvent Isotope Effect ([Diol] = 0.01 M; [QDC] = 0.001 M; [H_2SO_4] = 1.0 M; *T* = 323 K)

compound	10^4k_1 (s^{-1}) (H_2O)	10^4k_1 (s^{-1}) (D_2O)	k_{D_2O}/k_{H_2O}
1,2-cyclohexanediol	7.67	15.5	2.02
1,5-pentanediol	3.93	7.81	1.99

Table 4. Dependence of Rate Constants on Solvent Composition ([Diol] = 0.01 M; [QDC] = 0.001 M; [H_2SO_4 = 1.0 M; *T* = 323 K)

H_2O:AcOH (%, v/v)	100:0	95:5	90:10	85:15	80:20
dielectric constant (D)	69.94	66.76	63.59	60.41	57.23
10^4k_1 (s^{-1}) for:					
1,2-cyclohexanediol	7.67	7.93	8.25	8.80	9.46
1,5-pentanediol	3.93	4.06	4.22	4.50	4.84

Table 5. Effect of Temperature and Activation Parameters ([Diol] = 0.01 M; [QDC] = 0.001 M; [H_2SO_4] = 1.0 M)

	1,2-cyclohexanediol	1,5-pentanediol
T ± 0.1 K	10^4k_1 (s^{-1})	
313	3.81	1.94
318	5.75	2.88
323	7.67	3.93
328	11.4	5.79
333	15.5	7.91
$\Delta H^\ddagger$ (kJ mol^{-1})	57	60
$\Delta S^\ddagger$ (J K^{-1} mol^{-1})	−135	−129
$\Delta G^\ddagger$ (kJ mol^{-1})	101	102

Error limits: $\Delta H^\ddagger$ ±2 kJ mol^{-1}; $\Delta S^\ddagger$ ±3 J K^{-1} mol^{-1}; $\Delta G^\ddagger$ ±2 kJ mol^{-1}

Effect of Solvent Composition. The oxidation of diols by QDC was studied in solutions containing varying proportions of water and acetic acid. A decrease in the dielectric constant of the medium increased the rate of the reaction (Table 4).

Effect of Temperature. The oxidation of diols was studied at different temperatures, and the activation parameters were evaluated (Table 5).

Discussion

The activation parameters obtained were in agreement with literature values.[1,3] The values for the free energies of activation were nearly constant, indicating that the same mechanism operated for the oxidation of these diols.

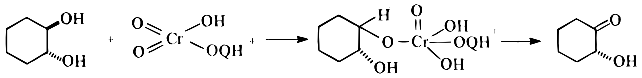
The linear increase in the rate of oxidation with acidity suggested the involvement of a protonated Cr(VI) species in the rate-determining step. Earlier reports have established the involvement of such Cr(VI) species in chromic acid oxidations.[12] Since the concentrations of acid used were in the range of 0.5 M to 2.0 M, the dichromate ion (and its protonated form) would be the predominant species. Moreover, the protonated Cr(VI) species would be a more reactive electrophile capable of increasing its rate of coordination to the diol.

The dielectric constants for water−acetic acid mixtures have been estimated approximately from the dielectric constants of the pure solvents. Plots of log k_1 against the inverse of the dielectric constant were linear ($r = 0.993$) with positive slopes, suggesting an interaction between a positive ion and a dipole.[13] The data in Table 4 indicated that the dielectric constants for water−acetic acid mixtures were a linear function of the solvent composition used in this investigation. This relationship between log k_1 and $1/D$ was thus obeyed in the range of dielectric constants used.

The rate of the acid-catalyzed reaction was greater in D_2O than in water ($k_{D_2O}/k_{H_2O} = 2.0$). The rate of an acid-catalyzed reaction would be expected to be faster in D_2O than in H_2O, when a preequilibrium protonation was involved.[14,15] The value of the solvent isotope effect suggested that the hydroxyl group was not involved either in the preequilibria or in the rate-determining step. Since the effect of changing the solvent was large, it effectively precluded the possibility of breaking an O−H bond in the rate-determining step. Hence, an ester mechanism became very probable.

There was no evidence for carbon−carbon bond fission upon the QDC oxidation of diols, in aqueous medium or aqueous acetic acid solutions. In the absence of products which would have resulted from the carbon−carbon bond fission, it would be reasonable to suggest that an acyclic mechanism must perforce operate in these oxidation reactions. The major portion of the diols was oxidized in the normal manner, CH(OH) → C=O. The fission of diols could not be effected in the presence of added free acid. Thus, the diols reacted with QDC to produce the corresponding α-hydroxy carbonyl compound, a pathway which has already been established to be energetically more favorable than that yielding the fission product.[3] The rates and the enthalpies would favor the formation of the hydroxy carbonyl product, similar to earlier investigations,[1,3] suggesting that the structure of the transition state was quite near to that of the products.

Scheme 1



There was no kinetic evidence for the formation of a cyclic intermediate in any appreciable concentration between the diols and QDC. The rate of oxidation, for example, was first order with respect to each reagent, for all the diols studied. The only evidence for the formation of a cyclic intermediate would depend upon the relation between the reaction rate and the configuration of the diol. An attempt was made to decipher a general correlation between the rate of oxidation by QDC and the proximity of the hydroxyl groups. Inspection of the kinetic data revealed that *trans*-1,2-cyclohexanediol reacted faster than 1,5-pentanediol by a factor of 1.95. The geometry of *trans*-1,2-cyclohexanediol was such that the two hydroxyl groups were in equatorial positions. The chromate substituent group was quite strained. There would be a rate-enhancing relief of steric strain in the transition state, and hence the decomposition of the chromate ester would be facilitated. The factor of 1.95 would thus represent the difference in the ease of ester decomposition. In 1,5-pentanediol, the hydroxyl groups were quite far apart. Hence, there would not be any possibility of a cyclic mechanism operating in the oxidation reactions of the diols under investigation.

The formation of α-hydroxy carbonyl compounds would suggest that the oxidation of diols by QDC simulated that of the oxidation of monohydric alcohols by chromic acid.[12] Cyclic ester formation involving both the hydroxyl groups was unlikely, and the mechanistic pathway would be an acyclic process through a chromate ester, which would then undergo decomposition (Scheme 1). This mechanistic sequence drew ample support from two excellent correlations:

(a) Periodic acid, lead tetraacetate and phenyliodosoacetate (used primarily to cleave 1,2-diols) do not readily oxidize simple alcohols or oxidize diols to α-hydroxy carbonyl compounds[3] (as do chromic acid or permanganate).

(b) The oxidative cleavage of 1,2-diols by periodate (the Malaprade reaction) is an allowed electrocyclic process, whereas the corresponding reaction of 1,2-diols by Cr(VI) is a forbidden process.[16] This excludes a cyclic mechanism and supports the view that the oxidation of diols by QDC would involve the conversion CH(OH) → C=O.

The data collected demonstrated that application of QDC to the oxidation of diols (vicinal and nonvicinal) led to the formation of α-hydroxy carbonyl compounds in good yields. This efficient reaction could thus prove to be a useful and general route in the synthesis of α-hydroxy carbonyl compounds.

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